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2017

### James Lind and the Disclosure of Failure

Stewart Justman

University of Montana - Missoula, [stewart.justman@umontana.edu](mailto:stewart.justman@umontana.edu)

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### Recommended Citation

Justman, Stewart, "James Lind and the Disclosure of Failure" (2017). *Global Humanities and Religions Faculty Publications*. 8.

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Stewart Justman  
Emeritus, University of Montana  
Missoula, MT 59812  
[Stewart.justman@umontana.edu](mailto:Stewart.justman@umontana.edu)

## James Lind and the Disclosure of Failure

The James Lind Library, an online repository of documents pertaining to the history and design of the clinical trial, records a number of cases in which a critic of the institution of medicine challenges the profession to a test of rival treatments. It was in this spirit that Bishop Berkeley (1685-1753) dared physicians to test their treatments for smallpox against his favored remedy, tar-water, under similar conditions. Like several other proposed trials of which we have a record, the tournament envisioned by Berkeley never took place. In the year of Berkeley's death, however, the world learned of an actual test of rival treatments under controlled conditions that had gone unreported and therefore unnoticed for half a decade.

This historic trial was conducted by James Lind (1716-94) in 1747 aboard HSM Salisbury in the English Channel. With scurvy already afflicting a ship out of port only a few weeks, Lind chose twelve patients 'whose cases were as similar as I could have them', divided them into pairs, and administered to each pair a possible treatment for the dreaded disease. Only the pair treated with oranges and lemons improved, even though the fruit supply ran out after six days.

Noteworthy in retrospect, Lind's trial was a non-event in its own time. Though its verdict in favour of citrus fruit agreed with what was already common maritime knowledge, Lind never followed up on it and never campaigned for controlled trials as a method of medical discovery. (After all, others had much to learn from his careful effort to hold experimental conditions constant.) In fact, after recounting the trial in the middle of his weighty *Treatise on the Scurvy*, Lind never mentions it again, and a quarter century later, in the Postscript to the third and final edition of the *Treatise*, he writes as if it never took place, concluding that scurvy has no definitive remedy, yields to 'very opposite methods of cure' and poses an enigma to medicine. In many cases, he observes, scurvy has such a grip on patients that it becomes 'a lasting affliction to them during a great part of their lives'—a chronic disease. In the Advertisement to the third edition he concedes, too, that the *Treatise* as it stands is marred by 'several seeming contradictions, which could not easily be avoided'. Far from claiming the honour of establishing a model of clinical investigation, he admits defeat, saying that he has reached a point where he can 'can carry my researches no further'.<sup>1</sup>

While the ready explanation for Lind's failure—that he got lost in the vapours of his own theories<sup>2</sup>—has some truth, it's also true that Lind was explicitly skeptical of theory and esteemed observation over intellectual guesswork.<sup>3</sup> ('Too high an opinion has been entertained of certain medicines [for scurvy] recommended by physicians at land, rather from a presumption founded on their theory of the disease, than from any experience of their effects at sea.') Lind probably interpreted the Salisbury trial as suggestive rather than probative, and it

may be that his belief in the efficacy of citrus (never absolute in the first place) weakened in later years because much of the scurvy he saw in Haslar hospital was hopelessly confounded with other diseases, or because he unwittingly destroyed vitamin C in the course of preparing his preferred remedy, a fruit concentrate known as 'rob'. In any case, scurvy as Lind observed it over the years challenged understanding, sometimes resolving with no change of diet or regimen, sometimes breaking out in those who eat a good diet and breathe good air. Moreover, in 'at least' ten or twelve percent of the cases seen by Lind at Haslar hospital, the disease proved stubborn, demanding not only dietary but medical treatment for weeks at a time, 'at the expiration of which, the injury done to the constitution was in many far from being removed'.

Unbeknownst to Lind, scurvy—a specific disease with a specific cure—lent itself perfectly to a clinical trial. That trials on less distinct and less treatable diseases would have advanced medicine seems doubtful. But what good would trials have done if unwanted outcomes could be buried in silence, as was the custom? Early proponents of clinical trials, from Petrarch to Van Helmont, from Bishop Berkeley to Mesmer, dreamed of public tournaments in which orthodox medicine would be put to shame. In the real world, rarely does medical investigation take place in such a public manner. Unlike doctors participating in a dramatic contest whose results play out for all to see, investigators in Lind's world were free to conceal adverse outcomes. Such a practice appeals directly to our bias in favour of positive findings as described by Francis Bacon: 'it is a proper and perpetual error in Humane Understanding, to be rather moved and stirred up by

affirmatives than by negatives, although in truth it ought to be indifferent to both.’<sup>4</sup>

At this point the high importance of Lind’s ethos of candour comes into focus.

Arguably, nothing but such an ethos could break through the robust practice of promoting ‘effective’ remedies by suppressing the record of their failures. As Ulrich Tröhler has shown, contemporaries of Lind who published statistical comparisons of rival medical methods breathed life into the concept of evidence itself by challenging that practice. One of their number, Robert Robertson, to whom Lind stood as a mentor, went so far as to document his own unsuccessful treatment of fevers in private practice, with great loss of life.<sup>5</sup> Other reformers objected in so many words to the concealment of failures, and in so doing they followed Lind, whose highest praise was for authors ‘of great candour and veracity’ and whose *Treatise* constitutes a unique tale of failure. ‘Lind, unlike . . . contemporary physicians then writing about scurvy, did not deliberately conceal evidence that ran counter to his own theories and observations.’<sup>6</sup>

Such candour was all the more crucial in that the practice of denying failure had deep roots. Even if a doctor rather than chance alone achieves a cure, wrote Montaigne in the latter 16<sup>th</sup> century, ‘how many times was it repeated?’<sup>7</sup> The implication seems to be that we will never really know, because doctors don’t let us in on their failures. Competing for credit as they do, why *would* they discuss failures? In Montaigne’s time, even as the era of exploration became the era of scurvy, ‘published case histories . . . often served quite unabashedly to show off the physician’s particular expertise and his skill in arriving at an unexpected explanation. Negative outcomes are rare and diagnostic or therapeutic errors on

the physician's part virtually non-existent.'<sup>8</sup> And this tradition of medical advertising, which impeded the conquest of failure because it blocked the recognition that failure has occurred, continued into Lind's time. The Navy's Sick and Hurt Board itself was pestered with immodest proposals for scurvy-remedies.<sup>9</sup> One reason the Admiralty was slow to provision British ships with lemons is that its interest fastened onto a diligently promoted rival, malt ('wort'). The darling project of Lind's contemporary, the physician David Macbride, wort theoretically cured a disease of defective fermentation by promoting the fermentation process in the body. However, any report from the sea that wort actually prevented or cured scurvy could only have been based on confusion, a willful erasure of the evidence of inefficacy, or both.

There are good reasons why it was scurvy that called forth Lind's confession of failure. He admitted that scurvy eluded his mastery and understanding because he couldn't pretend otherwise. The plague of the sea, scurvy took a fearful human toll and struck at the root of maritime power itself: the human beings who manned the ships. According to an account of Lord Anson's voyage excerpted by Lind, by the time the Gloucester reached the islands of Juan Fernandez (off the coast of Chile), it had lost three quarters of its crew to scurvy. The Centurion buried 292 of its original complement of 506. Such a scourge cried out for a remedy. In a memo to the Admiralty Gilbert Blane—physician to the West Indies fleet and a friend and disciple of Lind—pronounced oranges, lemons and limes an 'infallible' cure as well as preventive of scurvy.<sup>10</sup> Lind, who never believed scurvy had one and only one cause, found no treatment infallible, and what he saw or thought he saw at Haslar

hospital of the disease's behavior persuaded him that scurvy defeated the medical knowledge available to him. Not the acceptance of failure but belief in a remedy exempt from failure endangers the public good. 'It is perhaps the vain and chimerical belief of the existence of a never failing remedy for most diseases, which occasions the quick disgust which is conceived to medicine at every disappointment, and the daily attempts at new methods of cure, which has rendered the art of healing as variable and unconstant as our dresses.'

In the years after the publication of the final edition Lind's treatise, when quantifiers began to call for the accurate tabulation of medical outcomes (failures and all), a spirit of medical candour was in the air. Lind helped put it there. While such candour is certainly in the spirit of the Enlightenment and drew strength from that international movement, at least one of Lind's models of veracity precedes the 18<sup>th</sup> century. As part of his review of the scurvy literature, Lind reproduces at some length the eye-witness account by the physician Frederic Vander Mye of the siege of the city of Breda in 1625, in the course of which scurvy broke out. As a desperate ruse, the Prince of Orange let it be known that he was coming to the beleaguered soldiers' rescue by sending them a medicine 'of great price, but still of greater efficacy'. Three small vials were delivered, 'not enough for the recovery of two patients'. As a vehicle for 'the Prince's cure' (as it came to be called) and other makeshift medicines, the physicians prepared brews of herbs that 'now began to spring up above the ground'. The result of this orchestrated hoax was that despair was routed and 'many were quickly and perfectly recovered'—at least until scurvy flared up again, with lethal effect. Just one month after the Prince's miraculous

intervention, the city surrendered. (Characteristically, Lind wonders if the apparent recoveries could have been due to the antiscorbutic effect of the herbs used by the physicians to concoct their brews.)

Here then is another parable of failure. Indeed, Vander Mye's depiction of scurvy's behavior anticipates to some degree Lind's concept of the disease. Lind too finds that mental state has much to do with scurvy, such that dejection and melancholy predispose to it and cheerfulness guards against it. In the spirit of the Prince of Orange, Lind has used 'the most trifling prescriptions' to relieve scurvy, but while he has been able to give relief to some (not all) of the patients thus treated, he has also found that the disease itself persists. As in the story of Breda, Lind came to believe that the impression that we have solved or defeated scurvy is highly misleading—a mental mirage.

The story of the Prince's cure as relayed by Lind seems to have made a strong impression on some of his readers. William Falconer in his *Dissertation on the Influence of the Passions upon the Disorders of the Body* (1788) reproduces the account of the intervention of the Prince as well as Lind's comments on 'the passions of the mind' and attestation of Vander Mye's truthfulness. Yet Falconer fails to mention that scurvy had the last word at Breda; he leaves the impression that the charade of medical activity acted so powerfully on the imagination of the scurvy-stricken soldiers that they rose from their sick-beds and walked away from the disease itself. Elsewhere, however, Falconer objects to the practice of concealing failure. In his treatise on the medicinal value of Bath waters, he censures the 'suppression of unfavourable events and circumstances' in promotional literature.



Keenly aware of the unreliability of his knowledge, he is willing to say only that in many cases ‘a cautious trial’ of the waters is warranted.<sup>11</sup>

Lind’s quoted account the Prince’s cure re-appears in a historic pamphlet published in 1800 by John Haygarth. The tract in question, *Of the Imagination as a Cause and as a Cure of Disorders of the Body*, exposes the nullity of the then-popular Perkins ‘tractor’ by showing that patients tended to respond to a wooden replica just as they did to the genuine article—a modest instrument purportedly capable of removing pains from the body by the power of animal electricity. In confirmation of the surprising effects of the imagination on the body, Haygarth quotes the Breda episode from Lind’s treatise, along with Lind’s comments on it. Like Falconer, Haygarth for some reason neglects to mention that the Prince’s cure didn’t prevent the soldiers of Breda from succumbing en masse to scurvy in short order—an omission all the more surprising in that Haygarth goes on to comment that ‘I have sometimes observed that the administration of a new medicine. . . has been attended with great success—much greater than what was confirmed by future experience.’ That is just what happened in Breda. Like Falconer, too, Haygarth specifically objects to the concealment of failure in medical propaganda. (Significantly, in the report of his own trial four—not five—out of five subjects responded to a wooden instrument.) In publicity for the Perkins tractor itself, ‘cases which have been published are selected from many which were unsuccessful.’<sup>12</sup> Even an article as worthless as the Perkins tractor can be made to seem superbly effective if the ‘cures’ it produces by coincidence or the placebo effect are celebrated and its failures hushed.

In their disapproval of selective publication Falconer and Haygarth were not alone. Those who sought to reform medicine by the use of comparative statistics demanded accurate accounting, which in turn prohibits the concealment of adverse outcomes. The firebrand and first president of the London Medical Society, John Millar, maintained that 'by recording *every* case in a public and extensive practice, and comparing the success of various methods of cure, some useful information may be obtained.'<sup>13</sup> Robert Robertson, who like Lind began in the Navy as a surgeon's mate, published a detailed medical log of three journeys of HMS Rainbow in the 1770's, beginning with the case of a sailor treated unsuccessfully for intermittent fever—the first of many documented failures. Robertson cites Lind at many points, mentions meeting him to discuss the preventive use of Peruvian bark, and incidentally recounts a scurvy trial modeled on Lind's, which yields a result in favor of bark, not lime juice as we might have expected.<sup>14</sup> States William Withering in a classic study of digitalis printed a few years later, 'It would have been an easy task to have given select cases, whose successful treatment would have spoken in favour of the medicine [foxglove], and perhaps been flattering to my own reputation. But Truth and Science would condemn the procedure. I have therefore mentioned every case in which I have prescribed Foxglove, proper or improper, successful or otherwise.'<sup>15</sup> None of these works precedes publication of the final edition of Lind's treatise, crowned with the admission of defeat.

The unfortunate tradition of proclaiming success while burying failure carried into our own era. In 1981 a critic of medicine's evidence-base pointed out that 'Medical journals, along with those in other fields, tend to publish only reports

of “successful” interventions. One seldom reads of unsuccessful interventions, even though their frequency may be equal to, and probably greater than, those purported to be successful.’<sup>16</sup> The institution of the randomized clinical trial was supposed to settle medicine on a better evidentiary foundation than the tradition of ‘reports’ could possibly provide. However, the evidence from RCT’s is only as good as its publication, and few would now dispute that the medical literature has been distorted by the practice of selective publication.

Approximately 50% of randomized trials now go unpublished, presumably because they yielded the wrong result. Comments the source of this statistic, ‘With many powerful academicians, lobbyists, professional societies, funding agencies, and perhaps even regulators shifting away from trials to observational data, even for licensing purposes, clinical medicine may be marching headlong to a massive suicide of its scientific evidence basis. We may experience a return to the 18<sup>th</sup> century, before the first controlled trial on scurvy.’<sup>17</sup> But the scurvy trial changed nothing. What the times called for was the disclosure of failure, and this Lind encouraged not by oratory but the power of example. The concealment of trial data today not only distorts calculations of harm and benefit but subverts the practice that first enabled medicine to portray itself credibly as a progressive body of knowledge.

The author declares no conflict of interest

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